

Of Mice Men and (Lung) Cancer

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The Problem: Validating a mouse model of lung cancer at the molecular level. Given DNA expression data from a mouse model of lung adenocarcinoma, among a variety of human cancer expression data state the one most similar to the mouse model of adenocarcinoma. In addition, examine whether mutational effects in the human data might be related to the mouse model.

Motivation: Animal models of human disease serve as basic to our understanding and attempts at treatment of disease. Mouse models have been used extensively to study cancer. However, there has never been a genomic or molecular validation of the various mouse models developed. We performed the first molecular validation of a mouse model. The mouse model we focussed on is a mouse model of adenocarcinoma.

Previous Work: The mouse model of adenocarcinoma examined was a K-ras latent allele knock-in model [3]. The human datasets we looked to compare the mouse models were: two human lung cancer datasets [2, 1], and a human dataset with a wide variety of human tumor and normal tissues [4].

Approach: We first used a curated ortholog mapping between mouse and human genes to map the mouse and human datasets. We then used computational tools such as classification, gene set enrichment analysis [5], as well as mantel tests to make the comparisons.

Impact: We developed a procedure to validate a mouse model at the molecular level. The result of our analysis was to confirm that the mouse model of lung adenocarcinoma [3] was indeed most similar to human lung adenocarcinoma. In addition, we found that the mouse model is more similar to mutant K-ras human samples than wildtype K-ras samples.

Future Work: Genelists culled from this study will be examined to construct variants of the current mouse model. A similar analysis will be applied to mouse models of brain tumors and prostate cancer.

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